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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
02/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,132	ADAMS ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *136-154 and 156-159* is/are pending in the application.

4a) Of the above claim(s) *144-154* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136-143 and 156-159* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's amendment filed on 11/30/2009 has been entered. Claim 155 is canceled. Claims 158 and 159 are added. Claims 136-154 and 156-159 are pending. Claims 136-143 and 156-159 are currently under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Withdrawn Objections and/or Rejections

The rejection of claims 136-143 and 155-157 under 35 U.S.C. 112, first paragraph for written description is withdrawn.

Information Disclosure Statement

The information disclosure statement filed on 11/30/2009 has been considered by the examiner and an initialed copy of the form PTO-1449 is attached to the office action..

Drawings

Applicants argue that drawings were submitted with 371 applications and included on pages 165-171. Applicants are correct. However, Fig. 2 is objected to because the bars in the drawing cannot be clearly seen.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 136-143, 156, and 157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention. New claims 158 and 159 are also rejected on the same basis.

(iii). Response to Applicants' argument

Beginning at page 8 of Applicants' response, Applicants argue the following:

> The specification discloses the sequence of human RUP40 (SEQ ID NO:2), as well as the sequence of rat RUP40 (SEQ ID NO:4) and mouse RUP40 (SEQ ID NO:6). See ¶14 on page 4. The specification provides guidance for making constitutively active mutants of RUP40. See ¶68 on page 18. Specific allelic variants of human RUP40 are described in ¶69 on page 18, and in the sequence listing. RUP40 fusion proteins are described throughout the specification. See, e.g., pages 95-97. The specification also teaches that several techniques for making variants, e.g., by site-directed mutagenesis, PCR or direct synthesis, were generally available at the time of filing. See ¶390 on page 80 and ¶¶410 and 411 on page 90. The specification states that RUP40 is a GPCR that is coupled to Gq and increases the production of IP_3 when stimulated. See, e.g., ¶14 on page 4, ¶553 on page 133 and Fig. 5. The specification describes the general structure/function relationship of GPCRs. See, e.g, ¶5 on page 2 to ¶13 on page 4. The specification describes a variety of methods for assaying GPCRs which can be used to test variant proteins for activity. See the section starting on page 93 as well as page 132. The specification also describes a working example of a cell hypertrophy assay that employs RUP40, as well as a gene expression assay to assay ANF, which is induced by RUP40. See, Example 15 on page 133.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the human RUP40 set forth in SEQ ID NO: 2 is not disclosed as being constitutively active and the 136 does not require that GPCR variants or

homologues are constitutively active and possess any particular biological activity nor any particular conserved structure. One skilled in the art would not be able to identify an antagonist of the human RUP40 that inhibits hypertrophy in heart without a known ligand/agonist or using a constitutively active GPCR. Thus, it would require undue experimentation to make and use the claimed methods because one would have to determine first whether a particular GPCR that has at least 95% identity to amino acids 991 to 1364 of SEQ ID NO: 2 can be used to screen for an inhibitor of hypertrophy of a heart cell.

More importantly, since there is no nexus between (b) and (c), the claims, as written, encompass two unrelated methods: determining that the compound inhibits signaling by the G protein-coupled receptor and determining if the compound inhibits hypertrophy of a heart cell. However, the specification fails to provide guidance and working example to enable the broad methods.

Finally, it is pointed out that methods for assaying GPCRs that are used to test variants proteins for activity are not the same as methods of making the GPCRs used in the claimed methods.

At the second paragraph of page 9 of Applicants' response, referring to Exhibits A and B, Applicants argue that RUP40 is a member of an extremely well characterized family of proteins: GPCRs. Applicants argue that at the time of filing, the structure/function relationship of many GPCRs had been investigated. Applicants argue

that one of skill in the art would be make and use a large number of operable variants of RUP40 without undue experimentation.

Applicants' argument has been fully considered, but is not deemed to be persuasive because while many GPCRs are known in the art, each of the GPCRs has diversified structure and biological functions (see, e.g., J. Biol. Chem. 273:17299-17302, 1998). The knowledge of structure/function relationship of GPCRs does not provide specific guidance on how to make a GPCR that can be used in the instantly claimed method to identify an inhibitor to inhibit hypertrophy of a heart cell.

Beginning at the first paragraph of page 10, Applicants argue that claim 136 is directed to a screening method that employs a GPCR comprising an amino acid sequence having 95% identity to amino acids 991-1346 of SEQ ID NO: 2. Applicants argue that claim 136 also requires "determining that the compound inhibits signaling by said G protein-coupled receptor". Applicants argue that the claims require a GPCR that is both structurally and functionally defined. This is not persuasive for the reasons set forth above.

Beginning at the 3rd paragraph of page 10 of Applicants' response, Applicants cite case law and board decisions and argue that the crux of the question of enablement is whether practice of the claimed method would require undue experimentation. Applicants argue that given the guidance in the instant specification, the vast amount of structural information on GPCRs available in the prior art, the similarity of this case to

cases discussed in *Ex Parte Kubin, Ex parte Liao, Ex parte Heck and Ex parte Abad,* and limited scope of the claims, Applicants believe that one of skill in the art would be able to practice the claimed method without undue experimentation.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the fact pattern is different from those discussed in *Ex Parte Kubin, Ex parte Liao, Ex parte Heck and Ex parte Abad.* For example, in the case discussed in Ex Parte Kubin, claim 73 recites: "an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-"21 of SEQ ID NO: 2, wherein the polypeptide binds CD48". Claim 73 has a specific functional limitation, "wherein the polypeptide binds CD48". In contrast, claim 136 of the instant case does not recite a meaningful functional limitation for the GPCR variants.

At the 4th to fifth paragraphs of page 13 of Applicants' response, Applicants criticize a statement from the office action, "Without a known ligand/agonist, one skilled in the art would not be able to identify an antagonist of the human RUP40 that inhibits hypertrophy in heart". Applicants argue that the claims are directed to a method for identifying inhibitors of the recited GPCR, which includes, for example, inverse agonists as well as antagonists.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the specification does not disclose and Applicants do not explain how to identify an antagonist of the human RUP40 that inhibits hypertrophy in heart without a known ligand/agonist.

At the bottom of page 13 of Applicants' response, Applicants argue that Example 15 on page 133 of the instant specification presents experimental evidence showing that overexpression of wild type RUP40 stimulates hypertrophy of cardiomyocytes in the absence of a known ligand or agonist. This is not persuasive because, on one hand, Example 15 does not provide a valid example with respect to how to identify an inhibitor that inhibits hypertrophy in a heart cell. On the other hand, claim 136 does not require an overexpression of GPCR.

Accordingly, the instant disclosure fails to enable any person skilled in the art to make and use the claimed invention.

Claim Rejections under 35 USC§ 112, 2nd paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii). Claims 136-143 and 155-157 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 136-143 and 155-157 are indefinite because the claims do not have a preamble and the steps set forth in the methods are so ambiguous that they fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants have not address the issue in the response.

Claim Objections for Minor Informalities

Claims 136-143 and 155-157 are objected to because they recite non-elected species (species other than hypertrophic cardiomyopathy). Appropriate correction is required.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

February 23, 2010